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By: Printed: Lyza Fimular

APR 14 2003

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Hillman et al.

Title: PROTEINS ASSOCIATED WITH CELL PROLIFERATION

Serial No.: 09/894,657 Filing Date: June 28, 2001

Examiner: Harris, A. Group Art Unit: 1642

Commissioner for Patents  
Washington, D.C. 20231**RECEIVED**

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**SUBSTITUTE RESPONSE**  
**TO RESTRICTION REQUIREMENT UNDER 35 U.S.C. 121**

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Sir:

This paper is intended to replace the original paper filed in response to the Restriction Requirement and Request for Election dated December 2, 2002. Prior to examination of the application, please amend the specification of the above-identified application as listed below.

**IN THE SPECIFICATION**

Please replace the paragraph beginning at page 1 line 1, with the following rewritten paragraph:

This application is a divisional application of U.S. application Serial Number 09/410,372 filed on September 30, 1999, and issued on August 28, 2001, as U.S. Patent Number 6,281,334, entitled PROTEINS ASSOCIATED WITH CELL PROLIFERATION. That application is in turn a divisional application of U.S. application Serial Number 08/958,335 filed on December 4, 1997, and issued on June 27, 2000, as U.S. Patent Number 6,080,847, entitled PROTEINS ASSOCIATED WITH CELL PROLIFERATION. The contents of all of the foregoing patent applications and issued patents are hereby incorporated by reference.

For the Examiner's convenience, all pending claims are listed below. Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made."

1. An isolated polypeptide selected from the group consisting of:
  - a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5,
  - b) a naturally occurring polypeptide comprising an amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5,
  - c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5, and
  - d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5.
10. An isolated antibody which specifically binds to a polypeptide of claim 1.
29. A diagnostic test for a condition or disease associated with the expression of APOP in a biological sample comprising the steps of:
  - a) combining the biological sample with an antibody of claim 10, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex; and
  - b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.
30. The antibody of claim 10, wherein the antibody is:
  - a) a chimeric antibody,
  - b) a single chain antibody,
  - c) a Fab fragment,
  - d) a F(ab')<sub>2</sub> fragment, or
  - e) a humanized antibody.
31. A composition comprising an antibody of claim 10 and an acceptable excipient.

32. A method of diagnosing a condition or disease associated with the expression of APOP in a subject, comprising administering to said subject an effective amount of the composition of claim 31.

33. A composition of claim 31, wherein the antibody is labeled.

34. A method of diagnosing a condition or disease associated with the expression of APOP in a subject, comprising administering to said subject an effective amount of the composition of claim 33.

35. A method of preparing a polyclonal antibody with the specificity of the antibody of claim 10 comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5, or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibodies from said animal; and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5.

36. An antibody produced by a method of claim 35.

37. A composition comprising the antibody of claim 36 and a suitable carrier.

38. A method of making a monoclonal antibody with the specificity of the antibody of claim 10 comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5, or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibody producing cells from the animal;

c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells;

d) culturing the hybridoma cells; and

e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5.

39. A monoclonal antibody produced by a method of claim 38.

40. A composition comprising the antibody of claim 39 and a suitable carrier.

41. The antibody of claim 10, wherein the antibody is produced by screening a Fab expression library.

42. The antibody of claim 10, wherein the antibody is produced by screening a recombinant immunoglobulin library.

43. A method for detecting a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5 in a sample, comprising the steps of:

a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5 in the sample.

44. A method of purifying a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5 from a sample, the method comprising:

a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) separating the antibody from the sample and obtaining the purified polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:5.

51. An isolated antibody which specifically binds to a polypeptide of SEQ ID NO:3.

52. An isolated antibody which specifically binds to a polypeptide of SEQ ID NO:5.